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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/635,429	08/10/2000	Sachiko Machida	195617US0X	6992

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

RECEIVED: 4/21/04
OBLON, SPIVAK, McCLELLAND
MAIER & NEUSTADT, P.C.
DOCKETING DEPT.
Initials/Date Docketed: bp 4/22/04
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Due Date(s): 7/20/04

PTO-90C (Rev. 10/03)

Office Action Summary	Application No. 09/635,429	Applicant(s) MACHIDA ET AL.
	Examiner Abdel A. Mohamed	Art Unit 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2004*.

2a)☐ This action is FINAL. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-35,37-46 and 48-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-35,37-46 and 48-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF THE SUPPLEMENTAL AND APPEAL BRIEFS, AMENDMENT, STATUS OF THE APPLICATION AND CLAIMS

1. The request for reconsideration of Supplemental Appeal Brief filed 1/30/04, Supplemental Appeal Brief and Supplemental amendment filed 5/12/03 and Appeal Brief filed 3/31/03 are acknowledged, entered and considered. In view of Applicant's request (Supplemental Amendment filed 5/12/03) claims 36 and 47 have been canceled and claims 53 and 54 have been added. Thus, claims 31-35, 37-46 and 48-54 are now pending in the application. The rejections under 35 U.S.C. 103(a) over the prior art of record and 35 U.S.C. 112, second paragraph are withdrawn in view of Applicant's amendment and arguments filed 5/12/03. The Finality of the previous Office action is withdrawn in view of the following new ground of rejection:

CLAIMS REJECTION-35 U.S.C. § 103(a)

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 31-35, 37-46 and 48-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daugherty et al. (The Journal of Biological Chemistry, Vol. 273, No. 51, pp. 33961-33971, December 18, 1998) taken with Kitamura et al. (Macromol. Rapid Commun., Vol. 20, pp. 612-615, 1999) and Larsen et al. (Carbohydrate Research, Vol. 309, pp. 153-159, 1998).

The reference of Daugherty et al. discloses the application of an artificial chaperone refolding methods to porcine heart citrate synthase (CS), carbonic anhydrase B (CAB) and lysozyme by combining cyclic saccharide such as cyclodextrin and detergents such as POE(10)L, Triton X-100, SDS, etc. i.e., nonionic and ionic detergents (See e.g. pages 33961 and 33963-33964) as directed to claims 31-35, 37, 38 and 53. It is noted that the reference does not recite cyclic saccharide cycloamylose as currently claimed in claims 31 and 35; however, the reference recites cyclodextrin which is defined as a high molecular weight cyclic α-1,4-glucan which is referred as cycloamylose and generally called α, β and γ cyclodextrin, respectively. Thus, it is known in the art that cyclodextrin is the same as cycloamylose. For support, See e.g., particularly the reference of Machida et al. at page 131 (Machida et al. FEBS Letters, 486 (2000) 131-135) which was attached as pertinent art in the previous Office action

mailed on 8/13/02 as Paper No.6. Thus, the reference of Daugherty et al. discloses the combination of cyclic saccharide cycloamylose and detergents such as polyoxyethylenic detergent or ionic detergent such as SDS are useful as artificial chaperone.

The reference also teaches the use of the artificial chaperone refolding method to porcine heart citrate synthase wherein the folded protein has an α-helical structure or β-sheet structure or has an intramolecular S-S bond comprising of two steps, wherein the first step is to prevent aggregation of protein molecules by the formulation of protein-detergent complexes, in which hydrophobic regions of non-native protein molecules are shielded by detergent. The second step is the addition of cyclodextrin (cycloamylose) which initiates folding by stripping detergent from the protein-detergent complexes to facilitate the proper folding of protein into a correct higher-order structure with activity (See e.g. pages 33961, 33963-33964, 33966-33971 and Scheme I) as directed to claims 39-46, 48-52 and 54.

Although, the primary reference of Daugherty et al. clearly teaches the combination of cyclic saccharide cycloamylose and detergents such as polyoxyethylenic or ionic detergents is useful as an artificial chaperone and method for diluting the denaturant thereof and method of refolding denatured protein into native state having an activity by using the artificial chaperone as claimed in claims 31-35, 37-46 and 48-54. However, the reference differs from claims 31-35, 37-46 and 48-54 in not teaching the use of an artificial chaperone kit and the recitation of specific polymerization degree of cyclic saccharide cycloamylose. Nevertheless, the secondary reference of Kitamura et al. states that one of the remarkable properties of common cyclodextrins (α-, β-, and γ-

CD) is their ability to include small molecules (artificial chaperones) within their cyclic structure to form inclusion compounds. Most recently, large cyclodextrins with degrees of polymerization (DP) from 17 to several hundreds have been found as the result of the action of recombinant potato D-enzyme. These large CDs may have the potential to function as host molecules for a variety of organic reagents and iodine in a manner, which is different from the common cyclodextrins (See e.g., page 612, first paragraph, left column). Hence, describing cyclic saccharide cycloamylose (i.e., cyclodextrin) having a polymerization degree from 17 to several hundreds, and as such overlaps with the claimed ranges of polymerization degrees of claims 31, 33-35, 37-39, 41, 42, 46, 48, and 49. Further, the secondary reference of Larsen et al. on page 154, second paragraph, left column states that the large interest in cyclodextrins is based on their ability to form inclusion complexes with wide range of molecules. α-, β-, and γ-CD are capable to complex molecules ranging from gases to proteins and other biopolymers. CD is able to modify the physicochemical properties of the guest molecules by increasing their solubility and stability, as well as by modifying their reactivity. They have found numerous applications in the agricultural, food, chemical, and pharmaceutical industries. Furthermore, CD has been shown to be valuable as selectivity reagents for the resolution of structural, positional and stereoisomers in analytical chemistry. On page 156, the reference concludes by stating that using this method we have found that large CD have the ability to form complexes similar to the small CD (α-, β, and γ-CD). θ-CD gave the highest inclusion complex formation

constant among the larger CD. Thus, the secondary references discuss information on larger CD and their inclusion complex forming properties.

Therefore, it would have been obvious to one of ordinary skill in the art to apply the teachings of the secondary references of using different cyclodextrins (i.e., α-, β, and γ-CD) and their inclusion complex properties to the primary references teachings of protein refolding with cycloamylose because such features are known or suggested in the art, as seen in the secondary references, and including such features into the methods of the primary reference would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages of increasing the solubility, stability and modifying the reactivity of the molecules with which they can from inclusion complexes thereof.

In regard to the kit, the primary reference discloses an artificial chaperon formulation, however, from the cited references, it is conventional and within the ordinary skill in the art based upon the teachings of the combined references to have such kits/compositions as set forth in claims 31-35, 37, 38 and 53 since the combined references teach using these compositions together in the same formulations that would have been found in the claimed compositions and/or kits to formulate compositions into a kit format because the claimed kit is tailored for use in the claimed artificial chaperone kit formulation comprising the composition claimed. Hence, it would have been obvious to package the composition required for the method into kit format of the well-known commercial expediency of doing so.

Therefore, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated at the time the invention was made to employ an artificial chaperone kit comprising cyclic saccharide cycloamylose and polyoxyethylenic detergent or cyclic saccharide cycloamylose and ionic detergent and to a method for diluting the denaturant making the protein a denatured state by adding a specific detergent to a denatured protein, and preventing protein molecules from aggregation, thereafter adding cyclic saccharide cycloamylose, utilizing the inclusion ability thereof to strip detergent, accelerating the proper folding of protein into a correct higher-order structure activity, absence of sufficient objective factual evidence or unexpected results to the contrary.

CONCLUSION AND FUTURE CORRESPONDENCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The appropriate fax phone number for the organization where this application or proceeding is assigned arte (703) 3872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

AKM Mohamed/AAM

April 16, 2004

Christopher S. F. Low
CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
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